47. A method of vaccination of a human or animal body wherein the conjugate of claim 29 is administered to said human or animal body.

REMARKS

Reconsideration of this application is requested in view of the amendments to the specification and claims and the remarks presented herein.

The claims in the application are claims 29 to 47, all other claims having been cancelled. In addition, page 35 has been cancelled and a new Abstract of the Disclosure has been provided as required by the MPEP. It is requested that the formal drawings request be held in abeyance until there is an indication of allowable subject matter.

The disclosure was objected to as having no sequence identification number for the sequence set forth in lines 22 and 26 of page 28 and for not capitalizing the trademark on page 21.

Applicants respectfully request withdrawal of these grounds of objection. There is no sequence identification number on page 28 since the same sequence is a known sequence and is not part of Applicants' invention. The trademark Tween has been capitalized where appropriate and the expressions in claims 22 and 23 objected

to by the Examiner have been deleted. Therefore, withdrawal of this ground of rejection is requested.

It is noted that all of the claims were provisionally rejected under 35 USC 101 as not being patentably distinct from the claims of copending application Serial No. 09/405,986. It is requested that this rejection be held in abeyance until there is an indication of allowable subject matter in one of the two applications.

All of the claims were rejected under 35 USC 102 as being anticipated by the Bay et al reference. However, this is not a proper reference for the present application since it was not made available to the public until June 26, 1997 as can be seen from the letter of the editor of the Journal of Peptide Research submitted herewith. Applicants will supply a sworn English translation of the priority application to remove the same as a reference. Therefore, this ground of rejection is obviated.

Claims 1 to 5, 12, 13, 17, 18 and 22 to 25 were rejected under 35 USC 102(e) as being anticipated by the Chong et al patent and claims 1 to 5, 9, 12 to 14, 17, 18 and 20 to 25 were rejected under 35 USC 103 as being obvious over the Chong et al patent taken in view of the Zanini et al reference and claims 6 to 8 were rejected under 35 USC 103 as being obvious over the same combination of the prior art taken in further view of the Fung et

al reference. Claims 10 and 11 were rejected under 35 USC 103 as being obvious over the three references taken in further view of the Tam I and II references. The Examiner states that the Chong et al patent discloses a peptide conjugate comprised of a carrier comprising a dendrimeric polylysine to which a synthetic T cell epitope peptide is linked and a synthetic carbohydrate moiety of the fine chemical structure is linked to the said peptide which anticipates the indicated claims. The Zanini et al reference is cited to show in lines 27 to 31 of column 17 that a synthetic glycol conjugate may be used as a vaccine to induce immunity towards tumor cells which is not shown by the Chong et al patent. The Fung et al reference is cited to show the deficiency of the Chong et al patent in that the polysaccharide as containing galactose residue as indicated in claim 6 is shown by the Fung et al reference. The Tam I and II references are cited to show conjugates with several identical or different antigenic products of T cell antigens and B cell antigens joined to a dendritic polylysine to generate extremely high antibody titers. The Examiner concludes that Applicants' invention is obvious therefrom.

Applicants respectfully traverse these grounds of rejection since the Chong et al patent taken alone or in combination with the secondary, tertiary and quaternary references cited by the Examiner would not suggest Applicants' invention. New claim 29 shows the conjugate formulae which are described in Figure 1 and a variable parameter is introduced which consists of the number of lysine

residues that can be included in the polylysine dendrimeric structure. The support for the present terminology is found in lines 19 to 22 of page 7 wherein it is stated that a conjugate according to the invention comprises at least 3 lysine and at most 15 lysine covalently bonded one to each other. It is deemed that one skilled in the art would have no knowledge of the carbohydrate-peptide conjugate of claim 29 from the teachings of the Chong et al patent.

Chong et al relates to synthetic vaccines against Haemophilus influenzae (Hi) and discloses constructions which combine a polysaccharide derived from the Hi capsule consisting of a repeated polymer of polyribosyl ribitol phosphate (PRP) with synthetic peptides containing immuno dominant epitopes derived from outer membrane proteins (OMPs) from Hi. These OMPs are used both as antigens and as carrier molecules for PRP as can be seen from lines 55 to 60 of column 2. Figure 1 of the patent depicts several structures for the peptide carrier molecules used in the synthetic conjugates PRP-peptide and among the carrier molecules, there is described polylysine dendrimeric structures coupled to peptide antigenic determinates. In lines 38 to 43 of column 3, it is stated that one aspect of the Chong et al patent concerns the enhancement of carbohydrate immunogenicity by the use of MAP type constructions containing Hib determinant as carrier molecules for the carbohydrate moiety, more precisely, the PRP carbohydrate moiety.

In lines 29 to 39 of column 5 of the reference, it is stated that the invention encompasses the use of peptides consisting of immuno dominant epitope for T-cells as PRP carriers or as autologous or heterologous B-cell epitope carriers. However, Chong et al does not disclose the claimed carbohydrate peptide conjugate selected from the group consisting of the conjugates of Formulae B4-T4-M), (B2-T2-M) and (B8-T8-M) which are the object of claim 29.

Moreover, Chong et al is exclusively directed to the identification of new synthetic vaccines against antigenic determinants derived from Hemophilus influenza (Hi) and is not directed to precise structure of a peptide conjugate which may serve as a carrier molecule for the said antigenic determinants. As can be seen from Examples 1 to 11 of the reference, the inventors were first interested in the chemical synthesis of the PRP and not with the structural identity of the carbohydrate peptide conjugate, although the structure of several specific carbohydrate-peptide conjugates are described. However, there is no teaching whatsoever of the conjugates of claim 29 and therefore, Chong et al does not anticipate the claimed invention.

With respect to the obviousness type rejections, it is deemed that the combination of the prior art that the Examiner has made with the benefit of Applicants' disclosure would not render obvious Applicants' compounds either. The Chong et al reference is discussed above and the Zanini et al reference does not obviate the

deficiencies thereof. The Zanini et al reference discloses the structure of a multivalent molecule exhibiting multiple units of N-acetyllactosamine which is a recognized cancer associated carbohydrate. However, the Zanini et al article relates to the enhancement of the interactions between certain carbohydrates and proteins, the technical solution disclosed in Zanini et al dendrimeric constructions containing N-acetyllacetosamine to increase the density of these carbohydrates and to increase the probability of the binding of these carbohydrates with the proteins to which they bind.

The carbohydrate conjugates disclosed by the Zanini et al reference are not immunogenic compounds and do not contain any T-peptide epitopes. The Zanini et al reference only pertains to protein-carbohydrate interactions for inhibiting the binding of several viruses to their target cells which in a technical context is very different from the technical problems solved by Applicants' invention. Moreover, the Zanini et al reference is not interested in the recognition of the carbohydrate structures that they disclose by the proteins involved in the antigen receptors. Therefore, one skilled in the art would not combine the Zanini et al reference with the Chong et al reference to use the carbohydrates disclosed therein to form the conjugates described in Chong et al.

With respect to the combination with the tertiary reference

Fung et al, this does not overcome the deficiencies of the primary and secondary references. Fung et al discloses a conjugate composed of multiple copies of a carbohydrate antigen (TF hapten) which is coupled to the carrier protein KLH. The sole reason for which Fung et al has been cited by the Examiner is that it discloses a tumor-specific carbohydrate antigen which is conjugated to a peptide. However, the conjugate structures of Fung et al are completely different from the carbohydrate conjugate of Applicants' invention. It should be noted that the KLH carrier protein has been recognized for a long time as a model for coupling a wide variety of antigens against which a specific immune response was sought.

The high molecular weight of the KLH protein and its larger size has permitted successful immunization of laboratory animals against hapten peptides that are not immunogenic by themselves. Conjugates using KLH as a carrier protein induce a strong immune response against the carrier protein itself and it is not the case with a construct of a radical different conception represented by the MAG constructs of Applicants' invention wherein the different antigenic moieties are grafted to a low molecular weight polylysine skeleton endowed with weak immunogenicity or even a lack thereof.

The Examiner is in error when he combines such radically different teachings such as Fung et al et al and Chong et al and it should be noted that the induction of a specific immune response is

of a great complexity and has to date not been fully understood by researchers deeply involved in the field of immunology. One skilled in the art with the teachings of the references cited by the Examiner would have never deduced that the grafting of the synthetic tumor associated antigen conjugate of Fung et al would have been successfully used when grafted within the conjugates disclosed by Chong et al in view of the disparity of the teachings thereof. Therefore, the combination of the primary, secondary and tertiary references would not suggest Applicants' invention to one skilled in the art nor would one skilled in the art make such a combination.

With respect to the quaternary references of Tam I and II, it should be noted that these do not obviate the combination of the primary, secondary and tertiary references either. The latter two references have been discussed in the previous amendment and exclusively disclose peptide conjugates lacking any carbohydrate moiety. The MAP conjugates described by Tam I neither disclose nor suggest the synthesis of conjugates containing a polysaccharide moiety. The conjugates disclosed by Tam I and the claimed carbohydrate peptide conjugates are of radically different conception and structure. Moreover, Tam II discloses essentially the same conjugates as Tam I except that Tam II describes conjugates bearing a lipophilic membrane anchoring moiety for the MAP construct to be incorporated into liposome membrane before administration to the body. These teachings have absolutely

nothing to do with Applicants' invention. Therefore, withdrawal of these grounds of rejection is requested.

In view of the amendments to the specification and claims and the above remarks, it is believed that the claims clearly point out Applicants' patentable contribution and favorable reconsideration of the application is requested.

Respectfully submitted,
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Enclosures